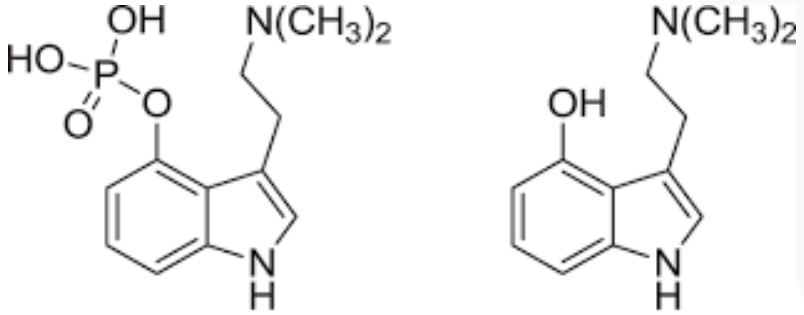
Semaglutide and Psilocybin in a Mouse Model of Obesity, Steatotic Liver Disease and Type 2 Diabetes

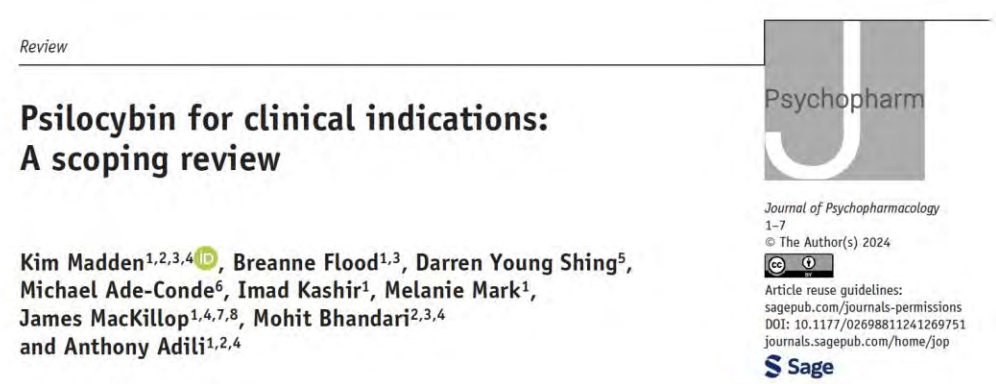
Sara De Martin, PhD

Psilocybin: a gift from mushrooms

- Psilocybin is a prodrug, psilocin is the drug



- The psychedelic effects of psilocybin are due to the agonism to the serotonin receptor 5-HT2A



Review

Psilocybin for clinical indications: A scoping review

Kim Madden[1,2,3,4], Breanne Flood[1,3], Darren Young Shing[5], Michael Ade-Conde[6], Imad Kashir[1], Melanie Mark[1], James MacKillop[1,4,7,8], Mohit Bhandari[2,3,4] and Anthony Adili[1,2,4]

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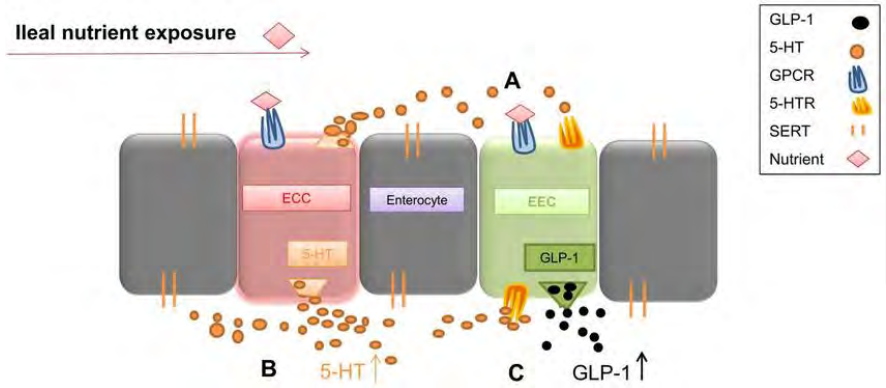
The serotonin/GLP-1 axis

- Serotonin and GLP-1 work together in the gut



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Journal of Nutritional Biochemistry

Nutrient-induced glucagon like peptide-1 release is modulated by serotonin

Dina Ripken[a,b,c,*], Nikkie van der Wielen[a,c], Heleen M. Wortelboer[b], Jocelijn Meijerink[c], Renger F. Witkamp[c], Henk F.J. Hendriks[a]

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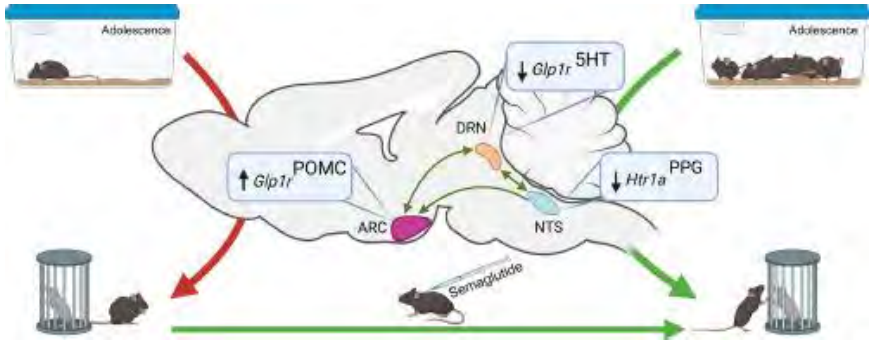
- GLP-1 modulates serotonin signaling in the CNS



Rozita H. Anderberg,[1] Jennifer E. Richard,[1] Kim Eerola,[1] Lorena López-Ferreras,[1] Elin Banke,[1] Caroline Hansson,[1] Hans Nissbrandt,[2] Filip Berqquist,[2] Fiona M. Gribble,[3] Frank Reimann,[3] Ingrid Wernstedt Asterholm,[1] Christophe M. Lamy,[4] and Karolina P. Skibicka[1]

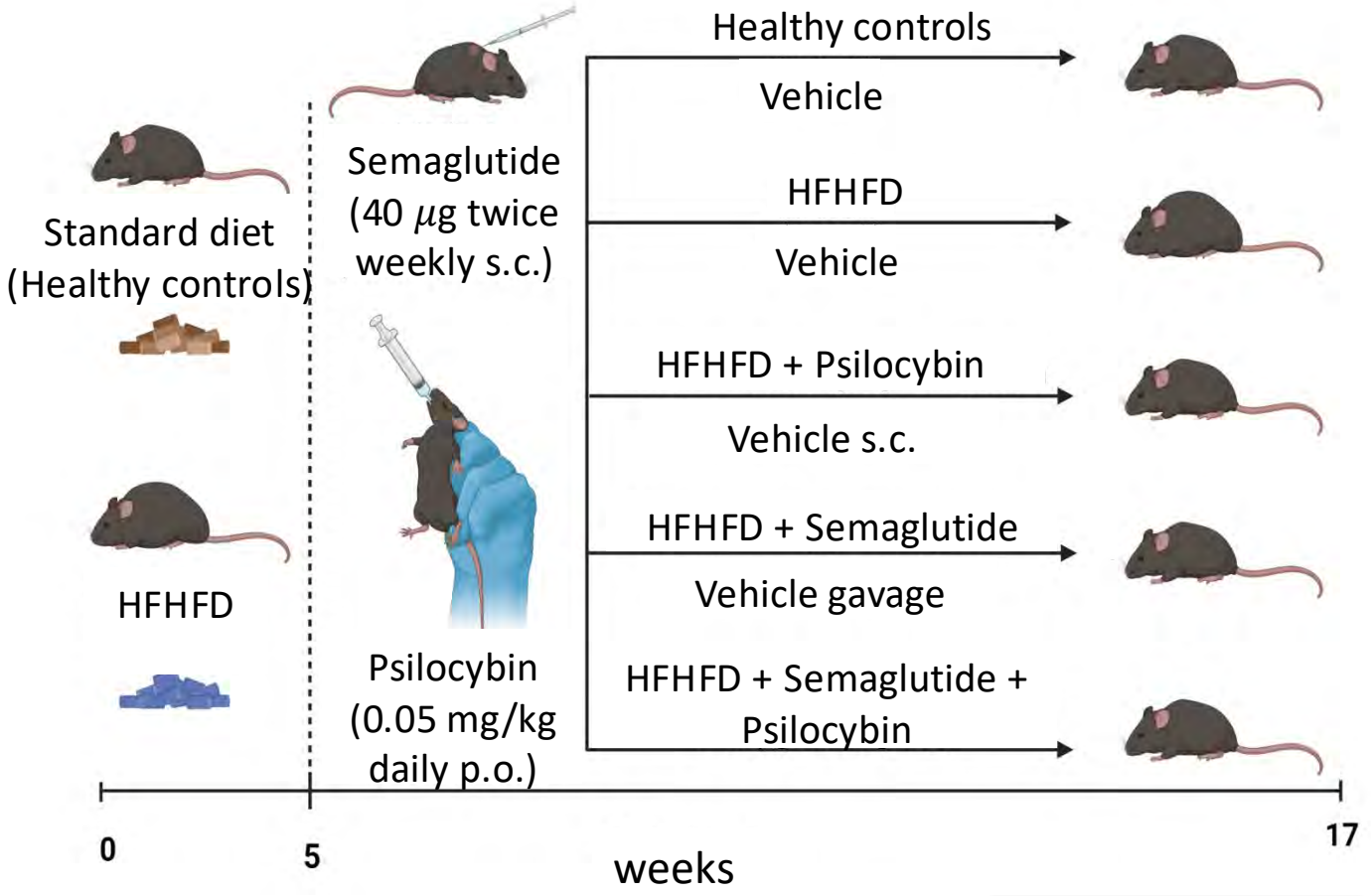
Check for updates

Glucagon-Like Peptide 1 and Its Analogs Act in the Dorsal Raphe and Modulate Central Serotonin to Reduce Appetite and Body Weight

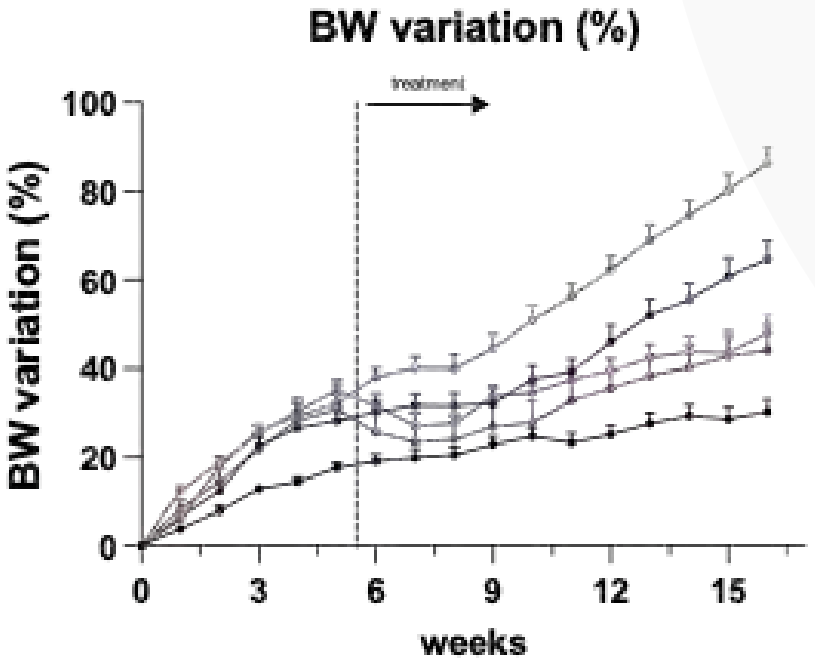
Diabetes 2017;66:1062–1073 | DOI: 10.2337/db16-0755

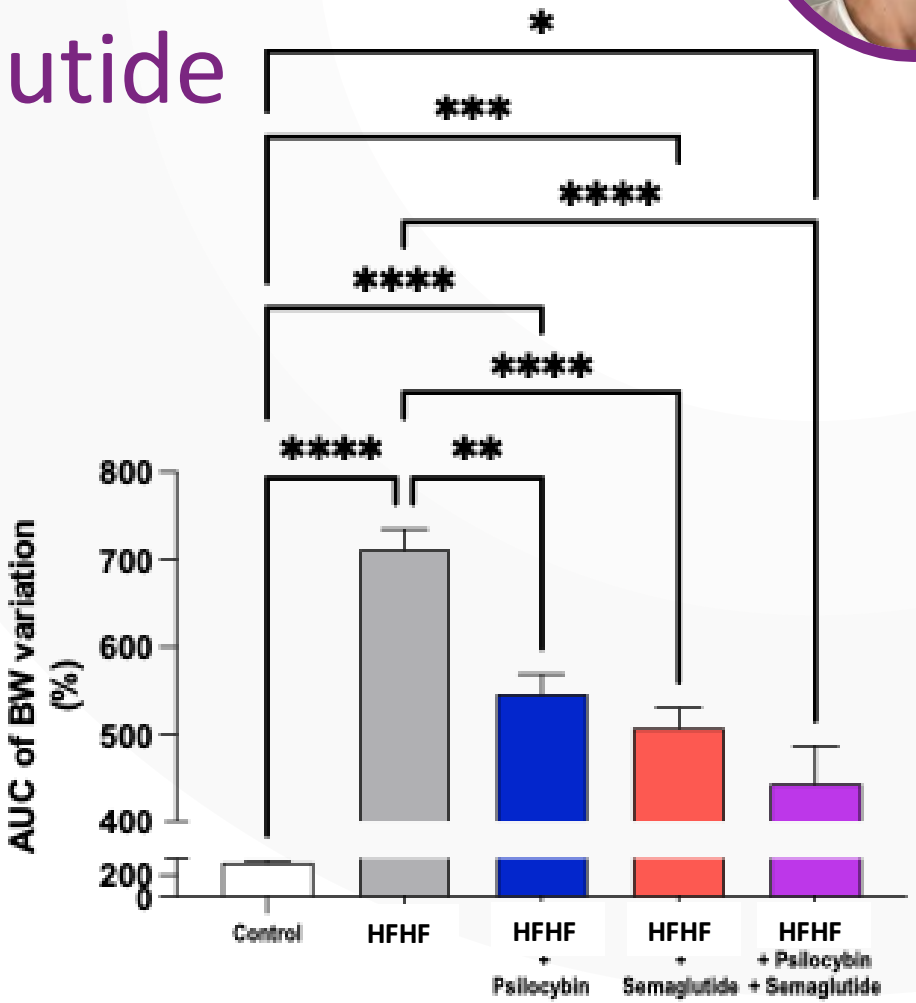
Pharmacological targeting of the serotonin/GLP-1 axis: our study protocol

- The study was performed by c57BL6 mice (n=10 per group)
- Metabolic disorders were induced by a high fat high fructose diet (HFHFD)



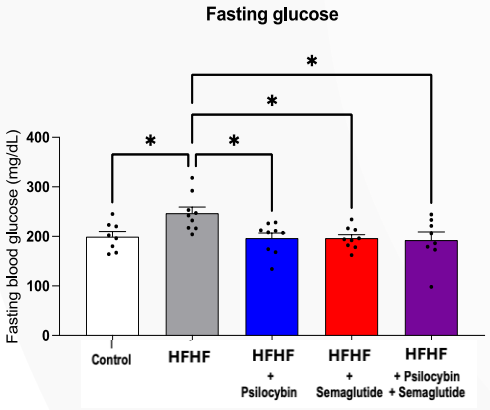
The increase of body weight is reduced by all treatments, especially by the combination psilocybin/semaglutide

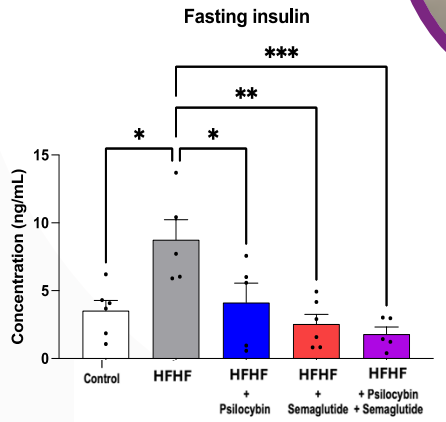




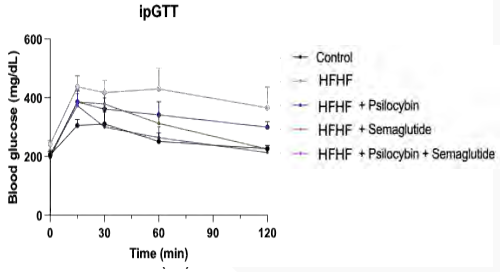
Positive effects on glucose homeostasis

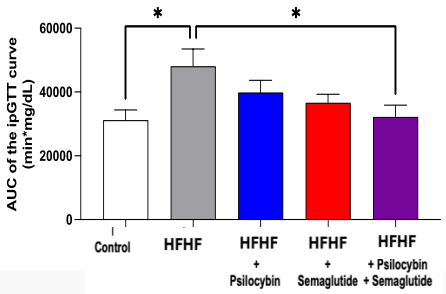
- Fasting glucose and insulin levels are normalized by all the treatments

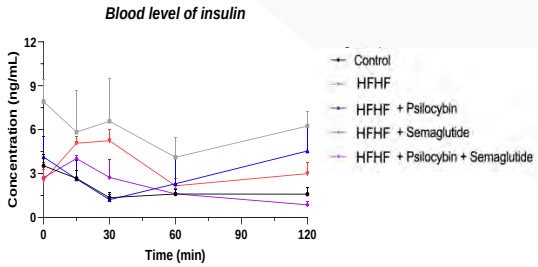


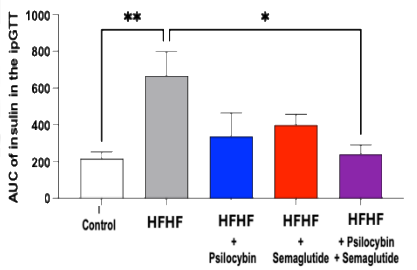


- Although all treatments are effective in ameliorating glucose curves in ipGTT, only the combination semaglutide/psilocybin leads to ipGTT glucose AUC normalization





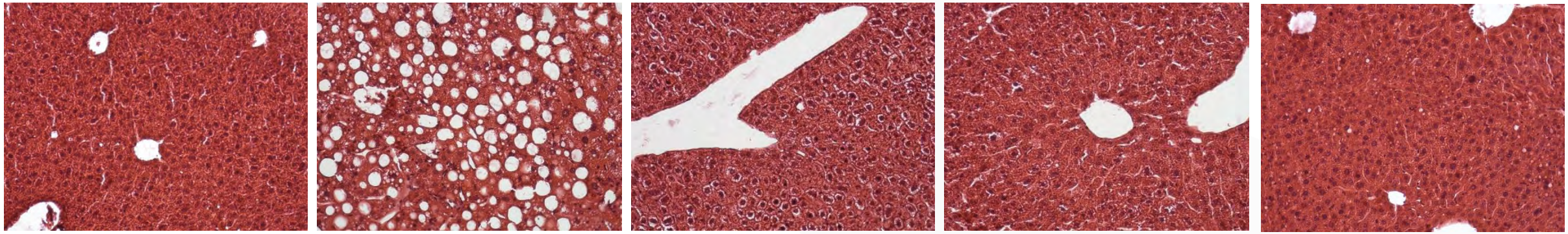


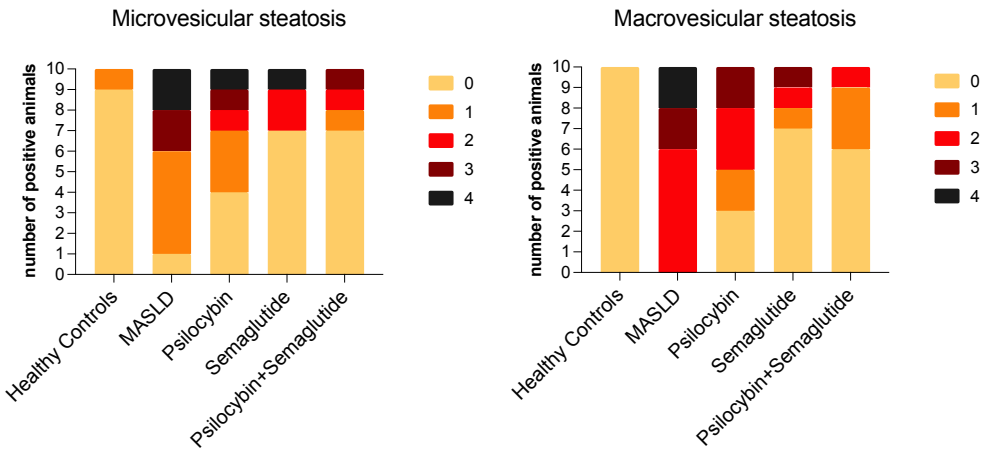


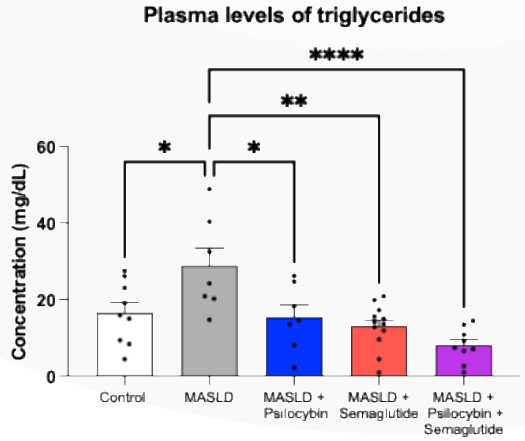
Liver steatosis is improved by all the treatments, more effectively by the combination of the two drugs

Control | HFHF | Psilocybin | Semaglutide | Psilocybin + Semaglutide

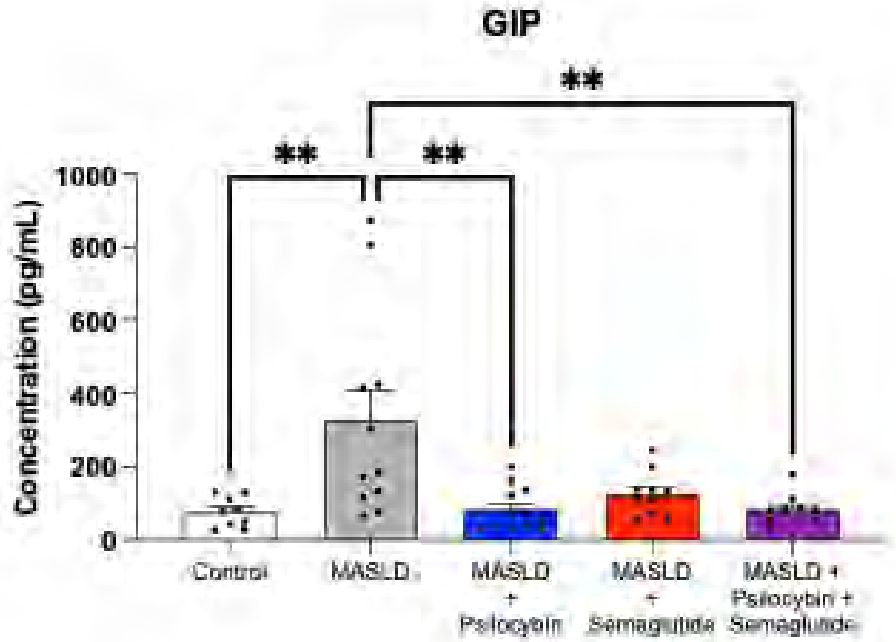
20X



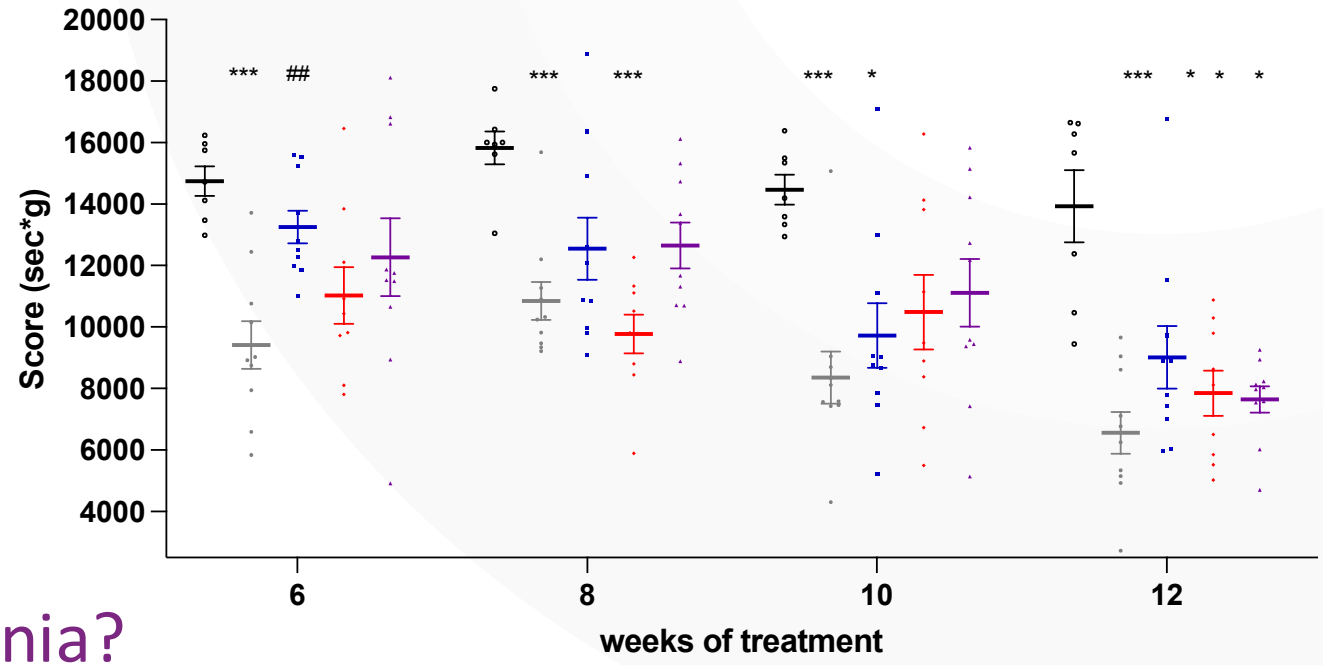




Psilocybin based therapies normalize plasma GIP levels



Psilocybin delays the HFHFD-induced loss of muscular function at the grid test



- Can psilocybin help sarcopenia?

Can leptin be involved in this effect?

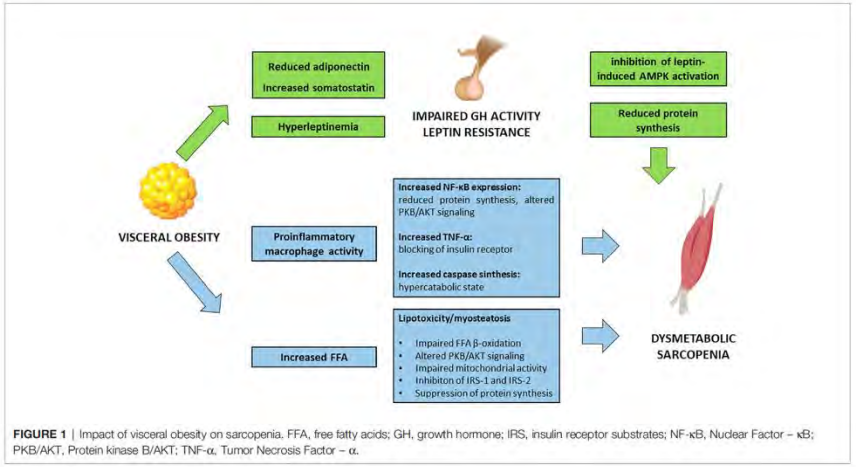
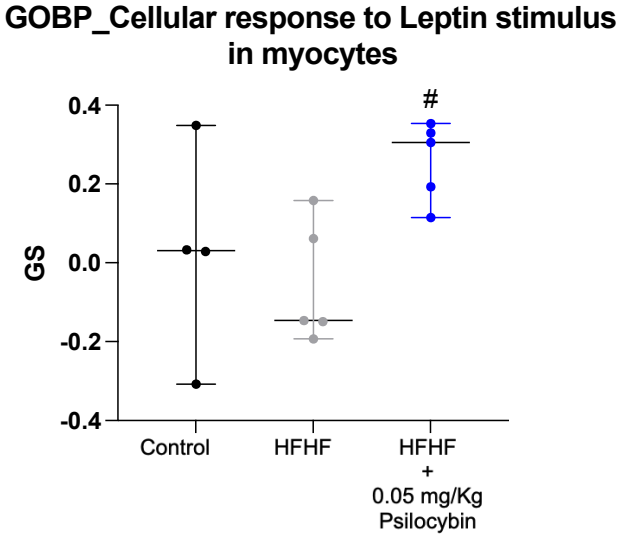
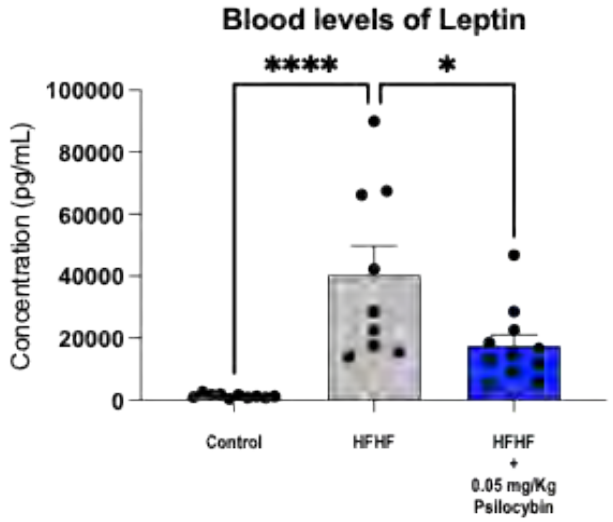
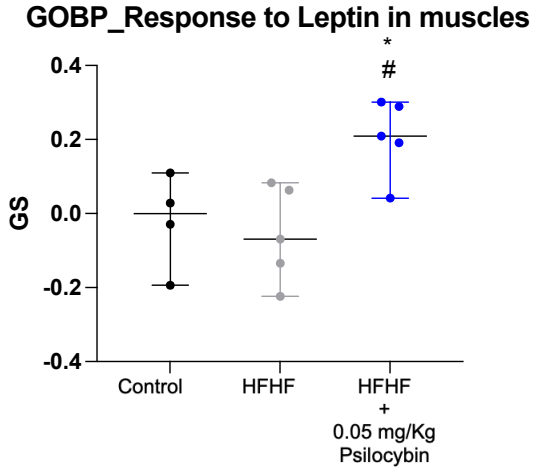


FIGURE 1 | Impact of visceral obesity on sarcopenia. FFA, free fatty acids; GH, growth hormone; IRS, insulin receptor substrates; NF-κB, Nuclear Factor – κB; PKB/AKT, Protein kinase B/AKT; TNF-α, Tumor Necrosis Factor – α.







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Leptin mediates the regulation of muscle mass and strength by adipose tissue

Kelsey H. Collins[1,2,3], Chang Gui[4,5], Erica V. Ely[1,2,3,4], Kristin L. Lenz[1,2,3], Charles A. Harris[6], Farshid Guilak[1,2,3,4] and Gretchen A. Meyer[1,3,4,5,7]

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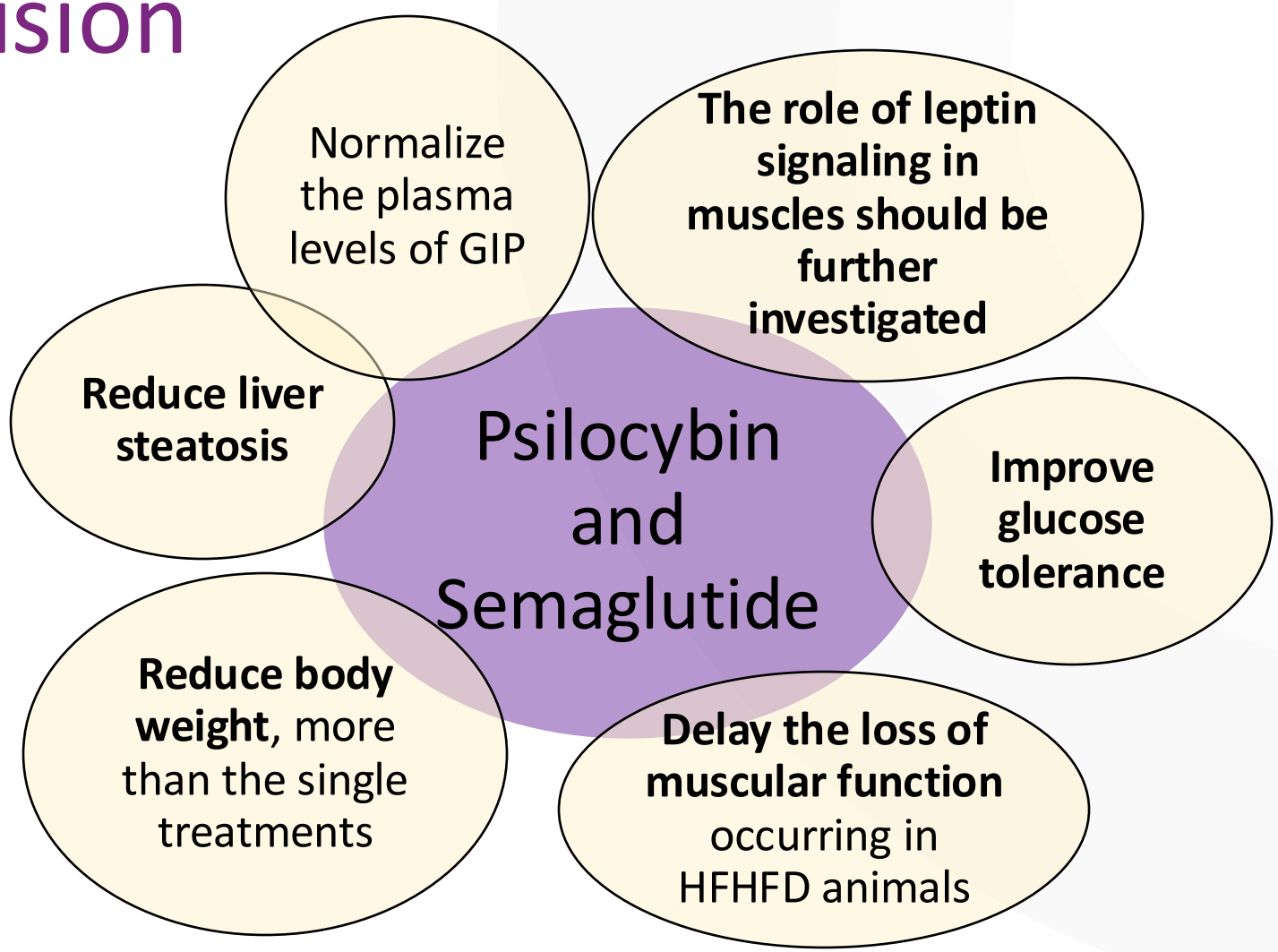
In conclusion



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Paolo Manfredi

and you for your attention!

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Q&A